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FILE 'REGISTRY' ENTERED AT 08:49:10 ON 27 SEP 2003

E ALPHA-1,2-FUCOSYLTRANSFERASE/CN

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SEA ALPHA-1,2-FUCOSYLTRANSFERASE

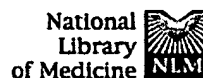
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QUE ALPHA-1,2-FUCOSYLTRANSFERASE

FILE 'CAPLUS, BIOSIS, SCISEARCH, EMBASE, MEDLINE, BIOTECHNO, ESBIODBASE, USPATFULL, LIFESCI, TOXCENTER, CANCERLIT' ENTERED AT 08:52:52 ON 27 SEP 2003

L3 0 S L1 AND RAT
L4 238 S L2 AND RAT
L5 105 S L4 AND (ISOLAT? OR PURIF?)
L6 6 S L5 AND (GM1 SPECIFIC)
L7 79 DUP REM L5 (26 DUPLICATES REMOVED)
L8 8 S L2 AND (GM1 SPECIFIC)
L9 4 DUP REM L6 (2 DUPLICATES REMOVED)
L10 6 DUP REM L8 (2 DUPLICATES REMOVED)



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☐ 1: J Biol Chem. 1992 Feb 5;267(4):2737-44.

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Purification of the secretor-type beta-galactoside alpha 1----2-fucosyltransferase from human serum.

Sarnesto A, Kohlin T, Hindsgaul O, Thurin J, Blaszczyk-Thurin M.

Wistar Institute of Anatomy and Biology, Philadelphia, Pennsylvania 19104-4268.

The secretor-type beta-galactoside alpha 1----2-fucosyltransferase from human serum was purified by hydrophobic chromatography on phenyl-Sepharose, ion-exchange chromatography on sulfopropyl-Sepharose, and affinity chromatography on GDP-hexanolamine-Sepharose. Final purification of the enzyme was achieved by high pressure liquid chromatography gel filtration and resulted in a homogeneous protein as determined by sodium dodecyl sulfate-polyacrylamide gel electrophoresis of the radiolabeled protein. The native enzyme appears as a molecule of apparent Mr 150,000 as determined by gel filtration high pressure liquid chromatography. The apparent Mr of the enzyme resolved in the presence of beta-mercaptoethanol by sodium dodecyl sulfate-polyacrylamide gel electrophoresis was determined to be 50,000, indicating a multisubunit structure of the enzyme. Secretor-type alpha 1----2-fucosyltransferase is a glycoprotein as determined by WGA binding properties. A comparison of the Mr of the native blood group H gene encoded with the secretor-type beta-galactoside alpha 1----2-fucosyltransferases as well as comparison of subunit Mr for both enzymes suggests structural similarity. The alpha 1----2 linkage formed between alpha-L-fucose and terminal beta-D-galactose by the purified H- and secretor-type alpha 1----2-fucosyltransferases was determined by 1H NMR homonuclear cross-irradiation analysis of the oligosaccharide products. The substrate specificity and Km values calculated from the initial rate using various oligosaccharide acceptors showed that purified enzymes differ primarily in affinity for phenyl-beta-D-galactopyranoside and GDP-fucose as well as type 1 (Gal beta 1----3GlcNAc), 2 (Gal beta 1----4GlcNAc), and 3 (Gal beta 1----3GalNAc) oligosaccharide acceptors. The secretor-type alpha 1----2-fucosyltransferase shows significantly lower affinity than the H enzyme for phenyl-beta-D-galactopyranoside and GDP-fucose as well as for type 2 oligosaccharide acceptors. On the contrary, type 1 and 3 oligosaccharide acceptors are preferentially utilized by the secretor-type enzyme as compared with the H enzyme. The enzymes also differ in several physicochemical properties, implying

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nonidentity of the two enzymes (Sarnesto, A., Kohlin, T., Thurin, J., and Blaszczyk-Thurin, M. (1990) J. Biol. Chem. 265, 15067-15075).

PMID: 1733969 [PubMed - indexed for MEDLINE]

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Sep 10 2003 12:34:08

L9 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 1998:516077 CAPLUS

DOCUMENT NUMBER: 129:258609

TITLE: Cloning and expression of the catalytic domain from
rat hepatoma H35 cell GDP-fucose:GM1
.alpha.1.fwdarw.2fucosyltransferase, an enzyme which
is activated during early stages of chemical
carcinogenesis in rat liver

AUTHOR(S): Sherwood, Anne L.; Holmes, Eric H.

CORPORATE SOURCE: Department of Cell Surface Biochemistry, Northwest
Hospital, Pacific Northwest Cancer Foundation,
Seattle, WA, 98125, USA

SOURCE: Archives of Biochemistry and Biophysics (1998),
355(2), 215-221

CODEN: ABBIA4; ISSN: 0003-9861

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A ganglioside GM1-specific

.alpha.1.fwdarw.2fucosyltransferase is induced during the early stages of
chem. carcinogenesis with N-2-acetylaminofluorene (AAF) in rat
liver hepatocytes. The induction of this enzyme gives rise to the
expression of a fucose-contg. ganglioside with the same determinant
structure as blood group B on a GM1 ganglioside core. Fucoganglioside
synthesis is not found in normal rat liver but is elevated in
pre-malignant liver and is often highly expressed in derived rat
hepatoma cell lines. Based upon the consensus sequence from portions of
previously cloned human, rabbit, and rat

.alpha.1.fwdarw.2fucosyltransferase enzymes, primers were designed which
were used in RT-PCR expts. with rat hepatoma H35 cell total RNA
to generate cDNAs encoding the extracellular, catalytic domain of the H35
cell .alpha.1.fwdarw.2fucosyltransferase. Sequencing of these PCR
fragments showed them to encode a novel enzyme with high homol. to other
cloned enzymes, particularly secretor .alpha.1.fwdarw.2fucosyltransferases.
The derived sequence indicated that the 3' portion of the gene was
virtually identical to the .alpha.1.fwdarw.2fucosyltransferase B (FTB)
fragment reported earlier in rat PROb colon-adenocarcinoma cells
(J-P. Piau et al. Biochem. J. 300, 623-626, 1994). A PCR product
corresponding to the H35 cell .alpha.1.fwdarw.2fucosyltransferase was
obtained from total RNA isolated from F344 rat liver
after 0.03% N-2-acetylaminofluorene administration. No PCR product was
obtained from total RNA isolated from normal F344 liver using
PCR primers for the H35 cell .alpha.1.fwdarw.2fucosyltransferase. The H35
cell .alpha.1.fwdarw.2fucosyltransferase was expressed in the pPROTA
vector and the derived fusion protein demonstrated the ability to transfer
fucose to ganglioside GM1 but not to the neolacto-series acceptor
nLcOse4Cer. (c) 1998 Academic Press.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2

ACCESSION NUMBER: 1990:133860 BIOSIS

DOCUMENT NUMBER: BA89:72671

TITLE: GDP-FUCOSE GM-1 ALPHA-1-2-
FUCOSYLTRANSFERASE IS ACTIVATED IN PARENCHYMAL
CELLS OF RAT LIVER DURING EARLY STAGES OF N-2
ACETYLAMINOFLUORENE INDUCED HEPATOCARCINOGENESIS.

AUTHOR(S): HOLMES E H

CORPORATE SOURCE: PACIFIC NORTHWEST RES. FOUND., 720 BROADWAY, SEATTLE, WASH.
98122, USA.

SOURCE: CARCINOGENESIS (LOND), (1990) 11 (1), 89-94.

CODEN: CRNGDP. ISSN: 0143-3334.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Gangliosides from liver parenchymal and non-parenchymal cells were isolated from Fischer 344 rats that had been fed normal diet or a diet supplemented with 0.03% N-2-acetylaminofluorene (AAF) for 4 weeks. Gangliosides from liver cell fractions were characterized by an induction of both II3NeuAcIV3.alpha.GalIV2FucGg4 and GM3 synthesis in the parenchymal cells of AAF-fed animals which were missing in parenchymal cells from animals fed normal diet. In addition, new bands corresponding to GM1 and GD1a were observed in cell fractions of AAF-fed animals. The activity of the GM1-specific .alpha.1.fwdarw.2fucosyltransferase induced after AAF feeding was found to be enriched 5- to 6-fold in the parenchymal cell fraction of AAF-fed animals and correlated with the parenchymal cell marker enzyme glucose-6-phosphatase in these cell fractions. Feeding animals the hepatotoxin acetaminophen at 1.87% in the diet for 10 weeks resulted in no increase in the levels of the .alpha.1.fwdarw.2fucosyltransferase. Antibodies specific for II3NeuAcIV3.alpha.GalIV2FucGg4 were produced and utilized in tissue localization studies. These results indicated little or no staining of normal liver tissue or that after acetaminophen feeding was observed. In contrast, focal areas of staining of liver tissue from animals after 3 weeks of 0.03% AAF feeding were readily apparent. These results indicate that induction of .alpha.1.fwdarw.2fucosyltransferase and fucoganglioside synthesis is most probably a property of liver parenchymal cells and is associated with events occurring during early stages of AAF-induced carcinogenesis.

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L10 ANSWER 1 OF 6 USPATFULL on STN

ACCESSION NUMBER: 2002:251220 USPATFULL

TITLE: Nucleic acids and proteins of a rat ganglioside
GM1-specific alpha
1-2 fucosyltransferase and
uses thereof

INVENTOR(S): Holmes, Eric H., Bothell, WA, UNITED STATES
Sherwood, Anne L., Mountlake Terrace, WA, UNITED STATES

| | NUMBER | KIND | DATE |
|-----------------------|--|------|---------------|
| PATENT INFORMATION: | US 2002137165 | A1 | 20020926 |
| APPLICATION INFO.: | US 2001-40863 | A1 | 20011101 (10) |
| RELATED APPLN. INFO.: | Division of Ser. No. US 1999-298886, filed on 23 Apr 1999, GRANTED, Pat. No. US 6329170 | | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | |
| LEGAL REPRESENTATIVE: | TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834 | | |
| NUMBER OF CLAIMS: | 62 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 10 Drawing Page(s) | | |
| LINE COUNT: | 2545 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A rat ganglioside GM.sub.1-specific .alpha.1.fwdarw.2fucosyltransferase is disclosed. Nucleotide sequences of a rat ganglioside GM.sub.1-specific .alpha.1.fwdarw.2fucosyltransferase, amino acid sequences of its encoded protein (including peptide or polypeptide), and derivatives thereof are described. Also described are fragments (and derivatives and analogs thereof) which comprise a domain of rat ganglioside GM.sub.1-specific .alpha.1.fwdarw.2fucosyltransferase with catalytic activity. Methods of production of rat ganglioside GM.sub.1-specific .alpha.1.fwdarw.2fucosyltransferase and derivatives and analogs thereof (e.g. by recombinant means) are provided. Methods of inhibiting the function of rat ganglioside GM.sub.1-specific .alpha.1.fwdarw.2fucosyltransferase (e.g. by means of antisense RNA) are provided. Methods of commercial scale use of the rat ganglioside GM.sub.1-specific .alpha.1.fwdarw.2fucosyltransferase in the production of fucosyl-saccharide compositions are described. Applications of these compositions, e.g. as additives for human nutritive compositions or immunotherapeutics for cancer, are disclosed.

L10 ANSWER 2 OF 6 USPATFULL on STN

ACCESSION NUMBER: 2002:235466 USPATFULL

TITLE: Nucleic acids and proteins of a rat ganglioside
GM1-specific alpha
1-2 fucosyltransferase and
uses thereof

INVENTOR(S): Holmes, Eric H., Bothell, WA, UNITED STATES
Sherwood, Anne L., Mountlake Terrace, WA, UNITED STATES

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 2002127655 | A1 | 20020912 |
| APPLICATION INFO.: | US 2001-999672 | A1 | 20011031 (9) |
| RELATED APPLN. INFO.: | Division of Ser. No. US 1999-298886, filed on 23 Apr 1999, GRANTED, Pat. No. US 6329170 | | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | |
| LEGAL REPRESENTATIVE: | TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834 | | |

NUMBER OF CLAIMS: 62
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Page(s)
LINE COUNT: 2921

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A rat ganglioside GM.sub.1-specific .alpha.1.fwdarw.2fucosyltransferase is disclosed. Nucleotide sequences of a rat ganglioside GM.sub.1-specific .alpha.1.fwdarw.2fucosyltransferase, amino acid sequences of its encoded protein (including peptide or polypeptide), and derivatives thereof are described. Also described are fragments (and derivatives and analogs thereof) which comprise a domain of rat ganglioside GM.sub.1-specific .alpha.1.fwdarw.2fucosyltransferase with catalytic activity. Methods of production of rat ganglioside GM.sub.1-specific .alpha.1.fwdarw.2fucosyltransferase and derivatives and analogs thereof (e.g. by recombinant means) are provided. Methods of inhibiting the function of rat ganglioside GM.sub.1-specific .alpha.1.fwdarw.2fucosyltransferase (e.g. by means of antisense RNA) are provided. Methods of commercial scale use of the rat ganglioside GM.sub.1-specific .alpha.1.fwdarw.2fucosyltransferase in the production of fucosyl-saccharide compositions are described. Applications of these compositions, e.g. as additives for human nutritive compositions or immunotherapeutics for cancer, are disclosed.

L10 ANSWER 3 OF 6 LIFESCI COPYRIGHT 2003 CSA on STN

ACCESSION NUMBER: 2002:69981 LIFESCI

TITLE: Nucleic acids and proteins of a rat ganglioside GM1-specific alpha 1-2fucosyltransferase and uses thereof

AUTHOR: Holmes, E.H.; Sherwood, A.L.

CORPORATE SOURCE: Northwest Hospital

SOURCE: (20011211) . US Patent: 6329170; US CLASS: 435/69.1; 435/243; 435/320.1; 435/325; 435/455; 536/23.1; 536/23.2; 536/23.5.

DOCUMENT TYPE: Patent

FILE SEGMENT: W3

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A rat ganglioside GM sub(1)-specific alpha 1-2fucosyltransferase is disclosed. Nucleotide sequences of a rat ganglioside GM sub(1)-specific alpha 1-2fucosyltransferase, amino acid sequences of its encoded protein (including peptide or polypeptide), and derivatives thereof are described. Also described are fragments (and derivatives and analogs thereof) which comprise a domain of rat ganglioside GM sub(1)-specific alpha 1-2fucosyltransferase with catalytic activity. Methods of production of rat ganglioside GM sub(1) -specific alpha 1-2fucosyltransferase and derivatives and analogs thereof (e.g. by recombinant means) are provided. Methods of inhibiting the function of rat ganglioside GM sub(1) -specific alpha 1-2fucosyltransferase (e.g. by means of antisense RNA) are provided. Methods of commercial scale use of the rat ganglioside GM sub(1) -specific alpha 1-2fucosyltransferase in the production of fucosyl-saccharide compositions are described. Applications of these compositions, e.g. as additives for human nutritive compositions or immunotherapeutics for cancer, are disclosed.

L10 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:772468 CAPLUS

DOCUMENT NUMBER: 133:331436

TITLE: Nucleic acids and proteins of a rat ganglioside GM1-specific

.alpha.1.fwdarw.2fucosyltransferase and synthetic uses

INVENTOR(S): Holmes, Eric H.; Sherwood, Anne L.

PATENT ASSIGNEE(S): Pacific Northwest Cancer Foundation, USA

SOURCE: PCT Int. Appl., 91 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2000064464 | A1 | 20001102 | WO 1999-US7384 | 19990423 |
| W: CA, JP | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |

PRIORITY APPLN. INFO.: WO 1999-US7384 19990423

AB A rat ganglioside **GM1-specific**

.alpha.1.fwdarw.2fucosyltransferase (I) is disclosed. Nucleotide sequences of a rat I, amino acid sequences of its encoded protein (including peptide or polypeptide), and derivs. thereof are described. Also described are fragments (and derivs. and analogs thereof) which comprise a domain of rat I with catalytic activity. Methods of prodn. of rat I and derivs. and analogs thereof (e.g. by recombinant means) are provided. Methods of inhibiting the function of rat I (e.g. by means of antisense RNA) are provided. Methods of com. scale use of the rat I in the prodn. of fucosyl-saccharide compns. are described. Applications of these compns., e.g. as additives for human nutritive compns. or immunotherapeutics for cancer, are also disclosed.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 1998:516077 CAPLUS

DOCUMENT NUMBER: 129:258609

TITLE: Cloning and expression of the catalytic domain from rat hepatoma H35 cell GDP-fucose:GM1 .alpha.1.fwdarw.2fucosyltransferase, an enzyme which is activated during early stages of chemical carcinogenesis in rat liver

AUTHOR(S): Sherwood, Anne L.; Holmes, Eric H.

CORPORATE SOURCE: Department of Cell Surface Biochemistry, Northwest Hospital, Pacific Northwest Cancer Foundation, Seattle, WA, 98125, USA

SOURCE: Archives of Biochemistry and Biophysics (1998), 355(2), 215-221

CODEN: ABBIA4; ISSN: 0003-9861

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A ganglioside **GM1-specific**

.alpha.1.fwdarw.2fucosyltransferase is induced during the early stages of chem. carcinogenesis with N-2-acetylaminofluorene (AAF) in rat liver hepatocytes. The induction of this enzyme gives rise to the expression of a fucose-contg. ganglioside with the same determinant structure as blood group B on a GM1 ganglioside core. Fucoganglioside synthesis is not found in normal rat liver but is elevated in premalignant liver and is often highly expressed in derived rat hepatoma cell lines. Based upon the consensus sequence from portions of previously cloned human, rabbit, and rat .alpha.1.fwdarw.2fucosyltransferase enzymes, primers were designed which were used in RT-PCR expts. with rat hepatoma H35 cell total RNA to generate cDNAs encoding the extracellular, catalytic domain of the H35 cell .alpha.1.fwdarw.2fucosyltransferase. Sequencing of these PCR fragments showed them to encode a novel enzyme with high homol. to other cloned enzymes, particularly secretor .alpha.1.fwdarw.2fucosyltransferases. The derived sequence indicated that the 3' portion of the gene was virtually identical to the .alpha.1.fwdarw.2fucosyltransferase B (FTB) fragment reported earlier in rat PROb colon-adenocarcinoma cells (J-P. Piau et al. Biochem. J. 300, 623-626, 1994). A PCR product corresponding

to the H35 cell .alpha.1.fwdarw.2fucosyltransferase was obtained from total RNA isolated from F344 rat liver after 0.03% N-2-acetylaminofluorene administration. No PCR product was obtained from total RNA isolated from normal F344 liver using PCR primers for the H35 cell .alpha.1.fwdarw.2fucosyltransferase. The H35 cell .alpha.1.fwdarw.2fucosyltransferase was expressed in the pPROTA vector and the derived fusion protein demonstrated the ability to transfer fucose to ganglioside GM1 but not to the neolacto-series acceptor nLcOse4Cer. (c) 1998 Academic Press.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2

ACCESSION NUMBER: 1990:133860 BIOSIS

DOCUMENT NUMBER: BA89:72671

TITLE: GDP-FUCOSE GM-1 **ALPHA-1-2-FUCOSYLTRANSFERASE** IS ACTIVATED IN PARENCHYMAL CELLS OF RAT LIVER DURING EARLY STAGES OF N-2 ACETYLAMINOFLUORENE INDUCED HEPATOCARCINOGENESIS.

AUTHOR(S): HOLMES E H

CORPORATE SOURCE: PACIFIC NORTHWEST RES. FOUND., 720 BROADWAY, SEATTLE, WASH. 98122, USA.

SOURCE: CARCINOGENESIS (LOND), (1990) 11 (1), 89-94.
CODEN: CRNGDP. ISSN: 0143-3334.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Gangliosides from liver parenchymal and non-parenchymal cells were isolated from Fischer 344 rats that had been fed normal diet or a diet supplemented with 0.03% N-2-acetylaminofluorene (AAF) for 4 weeks. Gangliosides from liver cell fractions were characterized by an induction of both II3NeuAcIV3.alpha.GalIV2FucGg4 and GM3 synthesis in the parenchymal cells of AAF-fed animals which were missing in parenchymal cells from animals fed normal diet. In addition, new bands corresponding to GM1 and GD1a were observed in cell fractions of AAF-fed animals. The activity of the **GM1-specific** .alpha.1.fwdarw.2fucosyltransferase induced after AAF feeding was found to be enriched 5- to 6-fold in the parenchymal cell fraction of AAF-fed animals and correlated with the parenchymal cell marker enzyme glucose-6-phosphatase in these cell fractions. Feeding animals the hepatotoxin acetaminophen at 1.87% in the diet for 10 weeks resulted in no increase in the levels of the .alpha.1.fwdarw.2fucosyltransferase. Antibodies specific for II3NeuAcIV3.alpha.GalIV2FucGg4 were produced and utilized in tissue localization studies. These results indicated little or no staining of normal liver tissue or that after acetaminophen feeding was observed. In contrast, focal areas of staining of liver tissue from animals after 3 weeks of 0.03% AAF feeding were readily apparent. These results indicate that induction of .alpha.1.fwdarw.2fucosyltransferase and fucoganglioside synthesis is most probably a property of liver parenchymal cells and is associated with events occurring during early stages of AAF-induced carcinogenesis.